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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,060	11/08/1999	James T Kealey	014/002C	6093

53456 7590 10/16/2006

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,060	KEALEY ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38 and 39* is/are allowed.

6)☒ Claim(s) *34-37,40 and 41* is/are rejected.

7)☒ Claim(s) *42 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *July 24, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed July 24, 2006.

Previously pending claims 27-33 have been canceled. New claims 34-43 are acknowledged.

Claims 34-43 are pending in the instant application.

Claims 34-43 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

Applicant's information disclosure statement filed July 24, 2006 is acknowledged. It is noted that the information disclosure statement lists a lone Office Action mailed to Applicant April 10, 2001. An office action is not a valid publication that can be printed on the face of a printed patent. Therefore, the Office Action has been considered, however, the Examiner has lined through the citation to prevent it from being printed on the face of the issued patent, in the event the instant application goes to issuance. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Response to Arguments

Applicants Amendment and Response filed July 24, 2006 has been considered. Rejections and/or objections not reiterated from the previous office action mailed January 25, 2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed January 25, 2006, claims 27, 28, 30, and 31 were rejected under 35 U.S.C. 103(a) as being unpatentable over Villeponteau et al. [U.S. Patent No. 5,776,679] in view of Skerra, A. (Nucleic Acids Research 1992 Vol. 20:3551-3554). **This rejection is moot** in view of Applicant's Amendment filed July 24, 2006. Specifically, this rejection is moot in view of Applicant's Amendment to cancel claims 27, 28, 30, and 31.

Applicant's Amendment's necessitated the new grounds of rejection presented below:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

> applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 34-36, 40, and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679].

Claim 34 is drawn to a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 137-196, nucleotide 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Claims 35, 36, 40, and 41 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein said polynucleotide has a sequence of about 10 to about 50 nucleotides that specifically hybridizes to the first nucleic acid sequence; wherein said polynucleotide has a sequence of about 15 to about 35 nucleotides that specifically hybridizes to the first nucleic acid sequence; and wherein said polynucleotide comprises a sequence of at least 7 nucleotide that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of a human telomerase (hTR), said accessible region being nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16.

It is noted that the instant specification at page 9, lines 25-33 recites, "Pharmaceutical composition" refers to a composition suitable for pharmaceutical use in a mammal. A pharmaceutical composition comprises a pharmacologically effective amount of an active agent and a pharmaceutically acceptable carrier. "Pharmacologically effective amount" refers to that amount of an agent effective to produce the intended pharmacological result. "Pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers, buffers, and excipients". Given this disclosure, the Examiner is interpreting the term, "pharmaceutical composition" to simply comprise a buffer.

Villeponteau et al. disclose the preparation of antisense plasmids for the RNA component of human telomerase using the following primer:

5'-GTTTGCTCTAGAATGAACGGTGGAAG-3' (see column 35, line 1, at primer R3C, which is 26 nucleotides in length). It is noted that the PCR reaction using primer R3C contained appropriate buffers as described at columns 32 and 33, lines 61-67 and 1-4, respectively. PCR primer R3C is reverse complementary to nucleobases 145-170 SEQ ID NO:16 of the instant invention. It is further noted that the reverse complimentarity between the PCR primer disclosed by Villeponteau et al. and nucleobases 145-170 of SEQ ID NO:16 is contiguous as it contains no mismatches. Given this high degree of complementarity, the PCR primer disclosed by Villeponteau et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed since the instant specification at page

10 lines 19 and 20 teaches, "a polynucleotide "specifically hybridizes" to a target polynucleotide if the polynucleotide hybridizes to the target under stringent conditions". It is noted that the instant specification at page 10, lines 20-26 describes "stringent conditions" to be generally, "the temperature and ionic conditions used in nucleic acid hybridization". Accordingly, the PCR primer disclosed by Villeponteau et al. would specifically hybridize to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed.

The burden of establishing whether the prior art primer disclosed by Villeponteau et al. has the further function of inhibiting the synthesis of telomeric DNA by telomerase as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the PCR

primer disclosed by Villeponteau et al. would or would not have the additional functional limitation of inhibiting the synthesis of telomeric DNA by telomerase under generally any assay condition.

Therefore, absent evidence to the contrary, claims 34-36, 40, and 41 are anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 34-37, 40, and 41 are rejected under 35 U.S.C. 103(a) as being anticipated by Villeponteau et al. [U.S. Patent No. 5,776,679, made of record in the Office Action mailed December 22, 2004] in view of Skerra, A. (Nucleic Acids Research 1992 Vol. 20:3551-3554, made of record in the Office Action mailed January 25, 2006).

Claim 34 is drawn to a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 137-196, nucleotide 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Claims 35-37, 40 and 41 are dependent on claim 34 and include all the limitations of claim 34 with the further limitations wherein said polynucleotide has a sequence of about 10 to about 50 nucleotides that specifically hybridizes to the first nucleic acid sequence; wherein said polynucleotide has a sequence of about 15 to about 35 nucleotides that specifically hybridizes to the first nucleic acid sequence; wherein said polynucleotide comprises a sequence of at least 7 nucleotide that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of a human telomerase (hTR), said accessible region being nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16; and wherein said polynucleotide comprises a nucleotide analog or non-naturally occurring nucleotide linkage selected from phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides and peptide-nucleic acids.

It is noted that the instant specification at page 9, lines 25-33 recites, "Pharmaceutical composition" refers to a composition suitable for pharmaceutical use in a mammal. A pharmaceutical composition comprises a pharmacologically effective amount of an active agent and a pharmaceutically acceptable carrier. "Pharmacologically effective amount" refers to that amount of an agent effective to produce the intended pharmacological result. "Pharmaceutically acceptable carrier" refers to any of the standard pharmaceutical carriers, buffers, and excipients". Given

this disclosure, the Examiner is interpreting the term, "pharmaceutical composition" to simply comprise a buffer.

Villeponteau et al. teach the preparation of antisense plasmids for the RNA component of human telomerase using the following primer:

5'-GTTTGCTCTAGAATGAACGGTGGAAG-3' (see column 35, line 1, at primer R3C, which is 26 nucleotides in length). It is noted that the PCR reaction using primer R3C contained appropriate buffers as described at columns 32 and 33, lines 61-67 and 1-4, respectively. PCR primer R3C is reverse complementary to nucleobases 145-170 SEQ ID NO:16 of the instant invention. It is further noted that the reverse complimentarity between the PCR primer taught by Villeponteau et al. and nucleobases 145-170 of SEQ ID NO:16 is contiguous as it contains no mismatches. Given this high degree of complementarity, the PCR primer taught by Villeponteau et al. meets the structural limitations of the claimed invention and would be expected to "specifically hybridize" to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed since the instant specification at page 10 lines 19 and 20 teaches, "a polynucleotide "specifically hybridizes" to a target polynucleotide if the polynucleotide hybridizes to the target under stringent conditions". It is noted that the instant specification at page 10, lines 20-26 describes "stringent conditions" to be generally, "the temperature and ionic conditions used in nucleic acid hybridization". Accordingly, the PCR primer taught by Villeponteau et al. would specifically hybridize to the accessible region of nucleotides 137-196 and/or nucleotides 137-166 of SEQ ID NO:16 as claimed.

The burden of establishing whether the prior art primer taught by Villeponteau et al. has the further function of inhibiting the synthesis of telomeric DNA by telomerase as instant claimed falls to Applicant. See (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977): "Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product... Whether the rejection is based on 'inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products [footnote omitted]. See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2122 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the PCR primer taught by Villeponteau et al. would or would not have the additional functional limitation of inhibiting the synthesis of telomeric DNA by telomerase under generally any assay condition.

Villeponteau et al. do not teach a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide further comprises a non-naturally occurring nucleotide linkage, including a phoshphorothioate linkage.

Skerra, A. teaches phosphorothioate-modified primers improve the amplification of DNA sequences by DNA polymerase with proofreading activity (see Abstract). Skerra, A. teaches the introduction of single phosphorothioate bond at the 3' termini of the PCR primer protects the oligodeoxynucleotide from exonuleolytic attack.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a polynucleotide comprising a sequence of at least 7 nucleotides that specifically hybridizes to an accessible region of the RNA component of human telomerase (hTR), wherein the accessible region is nucleotides 137-196 or nucleotides 137-166 of SEQ ID NO:16 of the instant invention as taught by Villeponteau et al. It would have been obvious to one of ordinary skill in the art to make the polynucleotide about 10 to about 50 or about 15 to about 35 nucleotides in length since the prior art taught those sizes were conventional in the art (see Villeponteau et al.).

One of ordinary skill in the art would have been motivated to have the pharmaceutical composition comprise a pharmaceutically acceptable carrier since the instant specification defines a pharmaceutically acceptable carrier as simply a buffer and it is well known in the art that PCR reactions comprise appropriate nucleotide primers, enzymes, buffers, and salts. One of ordinary skill in the art would have been motivated to modify the polynucleotide to include a phosphorothioate linkage since Skerra et al. teach the introduction of such linkages protects the oligodeoxynucleotide from exonucleolytic attack.

One of ordinary skill in the art would have expected success at making a pharmaceutical composition comprising a pharmaceutically acceptable carrier since the prior art taught the successful design and use of a polynucleotide pharmaceutical composition comprising a pharmaceutically acceptable carrier for use in amplifying DNA in a PCR reaction. One of ordinary skill in the art would have expected success at modifying the polynucleotide because Skerra, A. taught the successful design of a phosphorothioate-modified primer that improves the amplification of DNA sequences by DNA polymerase with proofreading activity.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing.

Conclusion

Claims 42 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 42 and 43 are considered free of the prior art since the prior art does not teach or fairly suggest a pharmaceutical composition comprising a polynucleotide in a pharmaceutically acceptable carrier, wherein the polynucleotide

(a) has a sequence of at least 7 nucleotides that specifically hybridizes to a first nucleotide sequence within an accessible region of the RNA component of human telomerase ("hTR"), wherein the accessible region is selected from nucleotides 290-319, and nucleotides 350-380 of hTR (SEQ ID NO:16),

(b) does not hybridize to a second nucleotide sequence within the template region of the hTR, said template region being nucleotide 46-55 of SEQ ID NO:16, and

(c) is effective to inhibit the synthesis of telomeric DNA by telomerase.

Allowable Subject Matter

Claims 38 and 39 are allowable. Claims 38 and 39 are considered to be free of the prior art since the prior art does not teach or fairly suggest a polynucleotide consisting of a sequence selected from the group consisting of SEQ ID NOs: 2-14 or pharmaceutical compositions therein.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tcg
October 10, 2006

SEAN McGARRY
PRIMARY EXAMINER
1635